

➤ ESANSİYEL TREMOR
monosemptomatik
midir?

tanım

- Tremor ile giden tablolar içinde en sık
- %5 >65 yaş
- Progresif 4-12 Hz postural ve kinetik tremor
- Zaman içinde;
Frekans azalır, amp artar,
İlaç yanıtı azalır,
Disabilite artar

Biraz tarih

- Galen of Pergamon (130-200AD)
- Sylvius de la Boe (1680)
- Van Swieten (1745)
- Charles Dana, NY' lu nörolog (1887)
- “Esansiyel” tremor 20. Yüzyılın ortalarında itibaren

Klinik özellikleri:

Essential tremor: Phenotypic expression in a clinical cohort

N.R. Whaley*, John D. Putzke, Yasuhiko Baba, Zbigniew K. Wszolek, Ryan J. Uitti

Department of Neurology, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32225, USA

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Abstract

Objectives: Examine the characteristics of an essential tremor (ET) clinical cohort including base-rate variability of several commonly accepted diagnostic criteria.

Methods: A clinical series of 487 consecutive individuals diagnosed with ET were included for study.

Results: The sample was 53% male, had a mean age of onset of 52, and a mean age of 71. Half of the sample had a family history of ET. Half presented with asymmetrical disease and tremor affected the arms (97%), voice (62%), and head or neck (48%). There was considerable variability in the base rate of individuals fulfilling various commonly used diagnostic criteria of ET.

Conclusion: The sample was deemed representative of ET clinical cohorts. Asymmetric disease was common, and there was considerable base-rate variation across traditional ET diagnostic criteria.

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Proportion of individuals fulfilling various diagnostics criteria

Criteria	<i>n</i> (%)
Tremor type	
Postural	441 (97)
Kinetic	445 (97)
Both	432 (94)
Distribution	
Head	219 (47)
Limbs	446 (97)
Both	209 (45)
Bilateral	
No	46 (10)
Yes	415 (90)
Duration	
1 or more years	467 (98)
5 or more years	358 (74)
10 or more years	209 (57)
Missing	4 (1)
Family history	
No	243 (50)
Yes	244 (50)
Conservative combination ^a	128 (27)

Proportion of individuals with various symptom characteristics at first clinical visit

	Overall sample ^a	Duration of 5 or more years and bilateral tremor ^b	Conservative combination ^c
	<i>n</i> (%)	<i>n</i> (%) 316 Δ	<i>n</i> (%) 128 Δ
Type			
Action tremor	445 (97)	308 (98)	125 (98)
Postural tremor	441 (97)	310 (98)	128 (100)
Resting tremor	65 (14)	48 (15)	24 (19)
Location			
Upper extremities	445 (97)	316 (100)	128 (100)
Head/neck tremor	219 (48)	171 (54)	80 (63)
Voice	286 (62)	208 (66)	90 (70)
Trunk	18 (4)	16 (5)	8 (6)
Chin	41 (9)	29 (9)	14 (11)
Lower extremities	40 (9)	30 (9)	15 (11)

- TRS ile hastalık süresi arasında anlamlı pozitif korelasyon: progresif bir hastalık
- Benzeri çalışmalar ile karşılaştırıldığında;
 1. Kadın-erkek oranı (ort %53 E)
 2. ETOH yanıtı (ort %52)
 3. Hastalık başlama yaşı (ort 46)
 4. ET (%39) ve PH (%8) açısından aile hikayesi pozitifliği

Table 6
Comparative demographic characteristics in population, epidemiological and clinical ET samples

Author	Sample size <i>n</i>	Males (%)	Age of onset (year)	ET family history (%)	PD family history (%)	ETOH responsive (%)
Whaley et al. (current)	487	53	52	50	9	59
Lou and Jankovic, 1991 [35]	350	51	40	63	20	67
Rajput et al., 1984 [36]	266	42		39	2	—
Rautakorpi et al 1982 [37]	194	66		—	—	—
Massey and Paulson, 1985 [38]	131	55		—	—	—
Larsson and Sjogren, 1960 [39]	81			—	—	—
Longe, 1985 [40]	35	80	37	29	—	31
Salemi, 1994 [41]	31	55		36	—	—
Hornabrook and Nagurney, 1976 [42]	175	27		18	1.7	—
Louis et al., 2000 [6]	115	66	54	—	—	73 ^a
Bharucha et al., 1988 [43]	233	46		—	—	—
Haerer et al., 1982 [44]	37	38		—	—	—
Average	178	53	46	39	8	52

Examine tremor location

Author	Location of tremor (%)					
	Arms	Head/neck	Voice	Legs	Trunk	Chin
<i>Clinic-based studies</i>						
Whaley et al. (present)	97	48	62	—	4	9
Lou and Jankovic, 1991[35]	90	41	17	14	2	7
Massey and Paulson, 1985 [38]	80	35	20	0.7	—	—
Longe et al., 1985 [40]	100	20	9	—	—	—
<i>Epidemiological studies</i>						
Louis, 2000 [10]	97	17	—	—	—	—
Rautakorpi et al., 1982 [3]	100	34	20	20	—	—
Larsson and Sjogren, 1960 [39]	100	23	19	9	4	—
Hornabrook and Nagurney, 1976 [42]	87	87	8	10	31	27
Average	94	38	22	11	10	14

Further evidence of genetic heterogeneity in familial essential tremor

Paolo Aridon^{a,b}, Paolo Ragonese^a, Maurizio De Fusco^b, Giuseppe Salemi^a,
Giorgio Casari^{b,c}, Giovanni Savettieri^{a,*}

^a*Dipartimento Universitario di Neuroscienze Cliniche, University of Palermo, Italy*

^b*Human Molecular Genetics Unit, San Raffaele Scientific Institute, Milan, Italy*

^c*Vita e Salute University, San Raffaele Scientific Institute, Milan, Italy*

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Abstract

Familial essential tremor (FET) is a common hereditary movement disorder with phenotypic variability and genetic heterogeneity. To date, linkage analyses revealed three loci associated to essential tremor (ET) (ETM1 on 3q13, ETM2 on 2p22-25, and a locus on 6p23). We performed a genetic analysis of these candidate chromosomal regions in a fifth-generation Italian kindred with autosomal-dominant ET. Of the 22 clinically evaluated family members, nine were affected by ET. The genetic study indicates that the ET in this family is not associated to any of the known ET loci. These findings support evidence of further genetic heterogeneity for such disease.

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Tani

Panel: Diagnostic criteria for definite ET

Consensus statement of the Movement Disorder Society on Tremor

Inclusion criteria

Bilateral postural tremor with or without kinetic tremor, involving hands and forearms, that is visible and persistent.
Duration >5 years.

Exclusion criteria

Other abnormal neurological signs (except Froment's sign)
Presence of known causes of increased physiological tremor
Concurrent or recent exposure to tremorogenic drugs or the presence of a drug withdrawal state.
Direct or indirect trauma to the nervous system within 3 months before the onset of tremor.
Historical or clinical evidence of psychogenic origins.
Convincing evidence of sudden onset or evidence of stepwise deterioration.

Deuschl G, Bain P, Brin M. Consensus statement of the Movement Disorder Society on tremor. Ad Hoc Scientific Committee. *Mov Disord* 1998; 13 (suppl): 2–23.

Overdiagnosis of essential tremor

A Schrag, A Muenchau, K P Bhatia, N P Quinn, C D Marsden

	Typical (n=25)	Atypical (n=25)
M/F	9/16	12/13
Median age, years (SD)	51 (19)	59 (18)
Median onset age, years (SD)	24.5 (20)	50 (22)*
Family history of hand tremor†	12 (57%)	8 (38%)
Response to alcohol†	8 (67%)	8 (67%)
Response to beta-blockers or primidone†	6 (50%)	3 (27%)
Head tremor	5 (33%)	14 (78%)*
Voice tremor	1 (6%)	4 (33%)
Leg tremor	4 (25%)	1 (8%)
Seen by MD specialist	7 (28%)	7 (28%)

MD=movement disorders. * $p < 0.05$, †in whom it was known.

Characteristics of patients with typical and atypical essential tremor

Common Misdiagnosis of a Common Neurological Disorder

How Are We Misdiagnosing Essential Tremor?

Samay Jain, MD; Steven E. Lo, MD; Elan D. Louis, MD, MS

Table 1. Demographic and Clinical Characteristics of Patients With False vs True ET*

Characteristic	Patients With False ET (n = 26)	Patients With True ET (n = 45)	Total Patients (N = 71)	P Value for True vs False ET
Age, y				
At current evaluation	57.3 (17.1)	65.4 (19.8)	62.4 (19.2)	.08
At tremor onset	43.5 (24.9)	44.9 (21.9)	44.4 (22.9)	.81
Duration of tremor, y	11.4 (13.9)	21.3 (17.3)	17.8 (16.8)	.02 ←
Female sex†	17 (65)	24 (53)	41 (58)	.32

Common Misdiagnosis of a Common Neurological Disorder

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Table 2. Factors From the Neurological History That Influenced the Odds of Having False vs True ET

Factor	Patients With False ET (n = 26)*	Patients With True ET (n = 45)*	OR (95% CI)†	P Value
Atypical distribution of tremor at onset‡ vs onset of tremor in both arms	21 (81)	20 (44)	5.3 (1.7-16.7)	.003
Current tremor distribution (by report)				
Head only	5 (19)	0	10.5 (1.3-95.4)§	.005
Both arms, head, and voice	8 (31)	34 (76)	0.1 (0.05-0.4)	<.001
Current reported tremor type				
Kinetic	12 (46)	39 (87)	0.1 (0.04-0.4)	.001
Postural	2 (8)	3 (7)	1.2 (0.2-7.5)	>.99
Rest	5 (19)	0	10.5 (1.3-95.4)§	.005
Tremor progression	23 (88)	38 (84)	1.4 (0.3-6.0)	.74
Family history of ET	2 (8)	13 (29)	0.2 (0.04-0.90)	.04
Ethanol responsiveness	6 (23)	15 (33)	0.6 (0.2-1.8)	.43

Hangi tremor tablolarıyla karışmış?

- %37 yanlış ET tanısı (1/3)
- Vakaları değerlendirenler kimler?

%88 nörolog

- En sık karışan tablo PH (%15 11/71),
distonik tremor (%8 6/71).

Review

Exploring the relationship between essential tremor and Parkinson's disease

Joohi Shahed*, Joseph Jankovic

Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Department of Neurology, 6550 Fannin, Suite 1801, Houston, TX, USA

Received 8 March 2006; received in revised form 16 May 2006; accepted 23 May 2006

- ET ve PH tanısında kullanılan veya tanıyı doğrulayan bir aracımız yok.
- Tanıyı klinik kriterlere göre koyuyoruz.
- Gördüğümüz tremorun fenotipini tanımlamak en önemli!
- Postural tremor, bazı PH olgularında fenomenolojik olarak ET' nin tremoruna çok benzer

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Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Department of Neurology, 6550 Fannin, Suite 1801, Houston, TX, USA

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- ET hastalarında eşlik eden PH' nı düşündüren özellikler:
 1. Rijidite, bradikinezi, poz instabilite
 2. Önceki postural/kinetik tremora eklenen yeni istirahat tremoru
 3. Mental konsantrasyon ile tremorun artması
 4. “re-emergent” tremor
 5. Çene veya dudak tremoru
 6. Semptomların asimetrisi

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Joohi Shahed*, Joseph Jankovic

Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Department of Neurology, 6550 Fannin, Suite 1801, Houston, TX, USA

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- **Koku duyusu deęişiklikleri:**
 - PH' da, olfaktor bulbustaki ve traktustaki Lewy body patolojisi
 - ET vakalarında tanımlandı (Louis 2003, Ondo 2005)
 - PH' larının %95' inde saptanan etkilenim, ET-istirahat tremoru olan vakalarda farklı sıklıkta

“ET-PH ayrı bir sendrom mu?”

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Joohi Shahed*, Joseph Jankovic

Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Department of Neurology, 6550 Fannin, Suite 1801, Houston, TX, USA

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- **Fonksiyonel görüntüleme;**

- **ET**

Striatal dopamin transporter ile

Kontrol grubu: PH ve sağlıklılar

Familial ETlerde dopaminerjik sistem anormallikleri daha fazla (Antonini 2005)

- **Visuo-motor koordinasyon testi bozuk 10 ET: 8/10 vakada erken PH bulguları (¹²³I-FP-CIT)**

Fonksiyonel nörogörüntüleme ET ve PH ayırımını yapar mı???

ET progrese oldukça nigrostriatal sistem disfonksiyonu ortaya çıkarak belirginleşiyor ve bazı hastalarda tremor gelişimine ve parkinsonial nörodejenerasyona dönüşüyor olabilir (Schwartz 2004).

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Joohi Shahed*, Joseph Jankovic

Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Department of Neurology, 6550 Fannin, Suite 1801, Houston, TX, USA

Received 8 March 2006; received in revised form 16 May 2006; accepted 23 May 2006

- **Patoloji çalışmaları:**
 - ET beyinlerinde Lewy body patolojisi (Yahr 2003, Louis 2005)
 - Louis 6/10 otopsi vakasında iki farklı paternde LB patolojisi buldu:
 1. 4/10 locus ceruleus > dorsal vagal n
 2. 2/10 idiyomatik PH' na tipik
 3. 4/10 serebellumda hafif dejeneratif değişiklikler

Review

Exploring the relationship between essential tremor and Parkinson's disease

Joohi Shahed*, Joseph Jankovic

Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Department of Neurology, 6550 Fannin, Suite 1801, Houston, TX, USA

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sonuç

- ET hastalarının çoğunluğu zaman içinde parkinsonial bulgular geliştirmez.
 - ET- alt grubu ----→ parkinsonial bozukluk
- Tremor dominant PH' larında önceden varolan veya eşlik eden ET sık rastlanıyor (Shahed 2005.....)
- ET fenotipinden PH fenotipine progresyon
 - Bu progresyonun belirleyicileri bilinmiyor?
- Dopaminerjik defisit / genetik

Patofizyoloji:

- Serebello-talamik yollardaki anormallik
- “cerebellar outflow” hastalığı
- Kinetik ve postural tremor dışında
 1. Kognitif bozukluklar (Gasparini 2001, Lombardi 2001)
 2. Postural instabilite ve ataksi (Stolze 2000, Deuschl 2000, Singer 1994)
 3. İst tremoru ve subklinik bradikinezi (Rajput 1993, Cohen 2002, Duval 2006)

Non-motor manifestations in essential tremor: Use of a validated instrument to evaluate a wide spectrum of symptoms

E.K. Tan^{a,c,d,*}, S. Fook-Chong^b, S.Y. Lum^a, C. Gabriel^a, K.K. Koh^e,
K.M. Prakash^{a,c}, Elan D. Louis^{f,g,h}

^a*Department of Neurology, Singapore General Hospital, Outram Road, Singapore, Singapore 169608*

^b*Department of Clinical Research, Singapore General Hospital, Outram Road, Singapore, Singapore 169608*

^c*National Neuroscience Institute, Outram Road, Singapore, Singapore 169608*

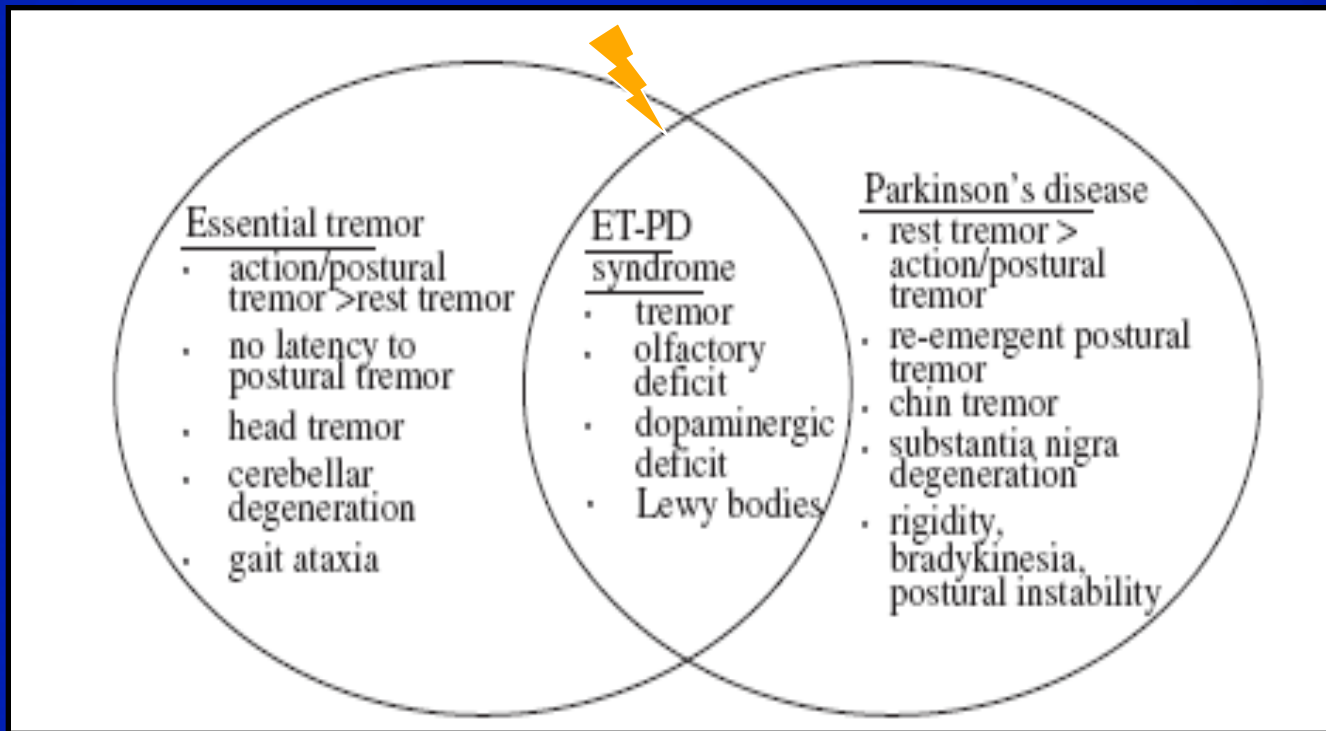
^d*SingHealth Research, Outram Road, Singapore, Singapore 169608*

^e*Healthway Medical, Outram Road, Singapore, Singapore 169608*

^f*Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Columbia University, NY 10032, USA*

^g*Department of Neurology, College of Physicians and Surgeons, Columbia University, NY 10032, USA*

^h*Taub Institute for Research on Alzheimer's Disease and the Aging Brain, College of Physicians and Surgeons, Columbia University, NY 10032, USA*



ET' da



- Tanıda ve takipte kullanılan / disabilite yaratan tek semptom TREMOR' dur.
- Progresif olduğuna dair klinik veriler vardır ancak,
- Yaygın nörodejeneratif tutulum ile ilgili yazılarda ET-PH sendromu vakaları bias oluşturabilir